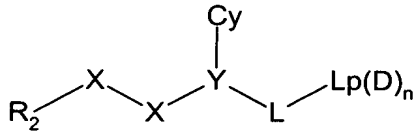
10/030188

JC03 Rec'd PCT/PTC 04 FEB 2002

**Clean Set of Claims**

1. (amended) A serine protease inhibitor of formula (I):



(I)

wherein:

$R_2$ is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachement of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, $MeSO_2$- or $R_1$, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or $R_{1j}$, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that $R_2$ cannot be aminoisoquinolyl;

each X independently is a C, N, O or S atom or a CO, $CR_{1a}$, $C(R_{1a})_2$ or $NR_{1a}$ group, at least one X being C, CO, $CR_{1a}$ or $C(R_{1a})_2$;

each $R_{1a}$ independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

$R_1$ is as defined for $R_{1a}$, provided that $R_1$ is not

contd. Cl

Sub B1

unsubstituted aminoalkyl;

Y (the α-atom) is a nitrogen atom or a $CR_{1b}$ group;

Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group, optionally substituted by groups $R_{3a}$ or $R_{3i}X_i$;

each $R_{3a}$ independently is $R_{1c}$, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkyloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein $X^3$ is O or S; and $R^{11}$ and $R^{12}$ are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or $-OCH_2O-$ which is bonded to two adjacent ring atoms in Cy;

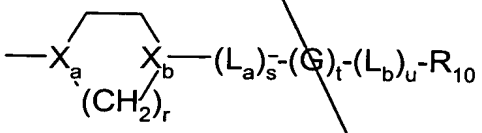
$X_i$ is a bond, O, NH or $CH_2$;

$R_{3i}$ is phenyl, pyridyl or pyrimidinyl optionally substituted by $R_{3a}$; and

$R_{1b}$, $R_{1c}$ and $R_{1j}$ are as defined for $R_{1a}$;

L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and

$Lp(D)_n$ is of the formula:



in which:

r is 1 or 2;

$X_a$ is CH and $X_b$ is N;

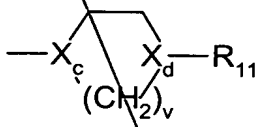
s, t and u are each 0 or 1;

$L_a$ and $L_b$ are each independently selected from a single bond, C=O, O and $NR_{1e}$, in which $R_{1e}$ is hydrogen or (1-

6C)alkyl;

G is (1-6C)alkanediyl; and

$R_{10}$ is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl; pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl {which is unsubstituted or substituted by one or two $R_3$ groups [wherein $R_3$ is hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, or haloalkyl]}, pyrrolinyl; or a group of formula:



in which v is 1,2 or 3; one of $X_c$ and $X_d$ is N and the other is CH or N (provided that when v is 1, $X_c$ and $X_d$ are not both N); and $R_{11}$ is hydrogen, (1-6C)alkyl or when $X_d$ is CH, hydroxy(1-6C)alkyl; provided that when t is 0, the sum of s and u is 1; when $X_b$ is N, $L_a$ is a bond or C=O; when $X_c$ is N, $L_b$ is a bond or C=O; when $X_b$ and $X_c$ are both N, t is 1; and when $(L_a)_s$-$(G)_t$-$(L_b)_u$ represents an alkyl group and $X_b$ and $X_c$ both represent N, the alkyl group contains at least two chain carbon atoms;

or $R_{10}$ is hydrogen and s, t and u are each 0;

contd. cl

or the compound of formula (I) that is 4-{[4-methoxybenzoyl-D,L-(2-trifluoromethylthiophenyl)-glycinyl]aminomethyl}-1-isopropylpiperidine;

but excluding the compound 4-[(3-ethoxybenzoyl-D,L-phenylglycinyl)aminomethyl]-1-[4-chlorobenzyl]piperidine;

or a physiologically-tolerable salt thereof.

Sch B(

2. (amended) A serine protease inhibitor according to claim 1, wherein:

$R_2$ is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachement of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, $MeSO_2$- or $R_1$, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or $R_{1j}$, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that $R_2$ cannot be aminoisoquinolyl;

each X independently is a C, N, O or S atom or a CO, $CR_{1a}$, $C(R_{1a})_2$ or $NR_{1a}$ group, at least one X being C, CO, $CR_{1a}$ or $C(R_{1a})_2$;

each $R_{1a}$ independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

$R_1$ is as defined for $R_{1a}$, provided that $R_1$ is not

contd. A1 Sub B1

unsubstituted aminoalkyl;

Y (the α-atom) is a nitrogen atom or a $CR_{1b}$ group;

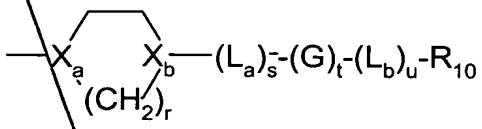
Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group optionally substituted by groups $R_{3a}$ or phenyl optionally substituted by $R_{3a}$;

each $R_{3a}$ independently is $R_{1c}$, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl; and

$R_{1b}$, $R_{1c}$ and $R_{1j}$ are as defined for $R_{1a}$;

L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and

$Lp(D)_n$ is of the formula:



in which:

r is 1 or 2;

$X_a$ is CH and $X_b$ is N;

s, t and u are each 0 or 1;

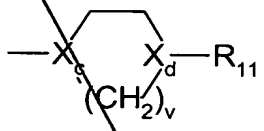
$L_a$ and $L_b$ are each independently selected from a single bond, C=O, O and $NR_{1e}$, in which $R_{1e}$ is hydrogen or (1-6C)alkyl;

G is (1-6C)alkanediyl; and

$R_{10}$ is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl;

contd. A1

pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl {which is unsubstituted or substituted by one or two $R_3$ groups [wherein $R_3$ is hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkysulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl]}, pyrrolinyl; or a group of formula:



in which v is 1, 2 or 3; one of $X_c$ and $X_d$ is N and the other is CH or N, provided that when v is 1, $X_c$ and $X_d$ are not both N; and $R_{11}$ is hydrogen, (1-6C)alkyl or when $X_d$ is CH, hydroxy(1-6C)alkyl; provided that when t is 0, the sum of s and u is 1; when $X_b$ is N, $L_a$ is a bond or C=O; when $X_c$ is N, $L_b$ is a bond or C=O; when $X_b$ and $X_c$ are both N, t is 1; and when $(L_a)_s$-$(G)_t$-$(L_b)_u$ represents and alkyl group and $X_b$ and $X_c$ both represent N, the alkyl group contains at least two chain carbon atoms,

or a physiologically-tolerable salt thereof.

Sub A1

3. (amended) A serine protease inhibitor according to claim 1, wherein $R^3$ is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, propyl, 2-propyl, butyl, 2-butyl, t-

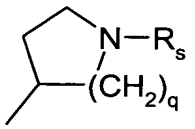
contd. cl

butyl, pentyl, 2-pentyl, 3-pentyl, isopropylaminomethyl, dimethylamino-methyl, diethylaminomethyl, dimethylaminoethyl, acetyl, hydroxymethyl, hydroxyethyl, carboxy, carboxy(1-5C)alkyl, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, aminocarbonyl, aminocarbonyl(1-5C)alkyl, methylamino, dimethylamino, ethylamino, formylamino, acetylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, isopropylsulphonyl, methylsulphenyl,1,2,4-triazol-2-yl, 1,2,4-triazol-4-yl, 1,2,3-triazol-4-yl, 1,3-imidazol-1-yl,1,3-imidazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, methylsulphonamido, ethylsulphonamido, propylsulphonamido, methylaminosulphonyl, ethylaminosulphonyl, propylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl and trichloromethyl.

Sub cl

4. (amended) A compound according to claim 1 wherein r is 2.

5. A compound according to claim 1 wherein $Lp(D)_n$ is of the formula:




wherein:

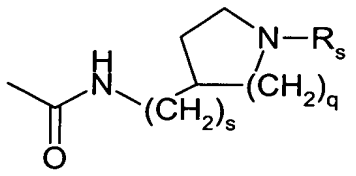
q is 1 or 2;

$R_s$ is hydrogen, $-(CH_2)_c-R_c$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [c is 0, 1 or 2; wherein $R_c$ is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, $SO_2NH_2$, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and $R_e$ and $R_f$ are independently hydrogen or $C_{1-3}$alkyl; or

$CHR_eR_f$ is (3-6C)cycloalkyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position, provided the substituent is not bonded to the CH group which is bonded to L), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl (which may bear a 1-methyl substituent), piperidinyl (which may bear a 1-methyl substituent) (provided that the tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and piperidinyl rings are not linked to the piperidin-1,4-diyl group through a ring nitrogen atom or a ring carbon atom adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-2-yl].

6. (amended) A compound according to claim 1 wherein L is CONH, $CH_2NHCO$, $CONHCH_2$, $CONHCH_2CH_2$ or $CON(Me)CH_2$.

7. A serine protease inhibitor according to claim 2 wherein -L-$Lp(D)_n$ is of the formula:



wherein

q is 1 or 2;

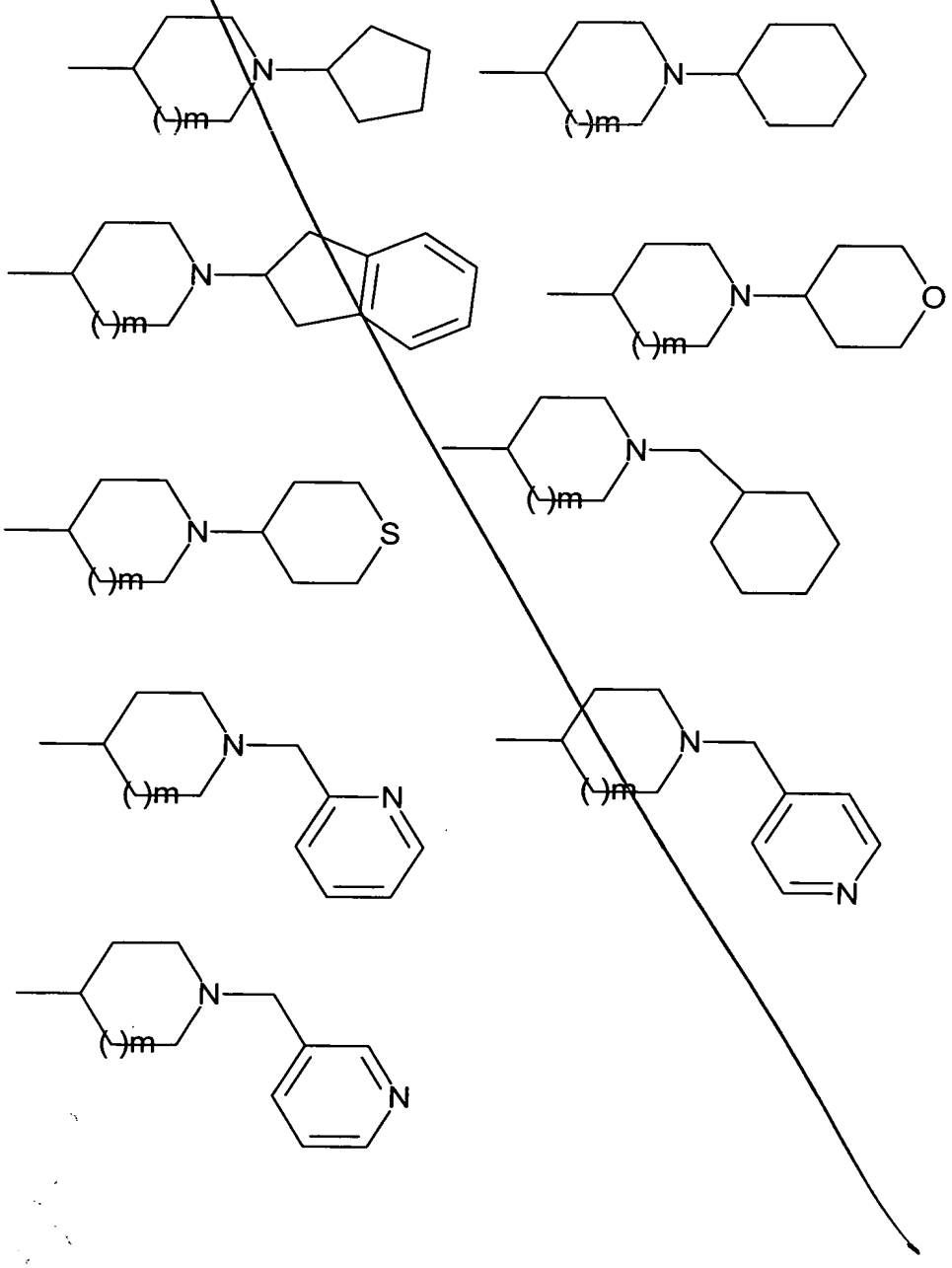
s is 0 or 1; and

$R_S$ is $-(CH_2)_c-R_C$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [wherein c is 1 or 2; $R_C$ is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, $SO_2NH_2$, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and $R_e$ and $R_f$ are independently hydrogen or $C_{1-3}$alkyl; or $CHR_eR_f$ is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or

hydroxymethyl substitutent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

8. (amended) A compound according to claim 5 wherein q is 2.

9. (amended) A compound according to claim 1 wherein $Lp(D)_n$ is selected from one of the following formulae:



contd. Q3

wherein m represents 0 or 1.

Sub B1

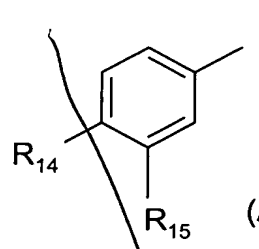
10. (amended) A compound according to claim 7 wherein $R_S$ is selected from: hydrogen, methyl, ethyl, prop-2-yl, but-2-yl, pent-3-yl, hept-4-yl, cyclopentyl, cyclohexyl, cyclohexylmethyl, 1-methylpiperidin-4-yl, tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, phenyl, benzyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrid-3-ylmethyl, pyrid-4-ylmethyl and indan-2-yl.

11. (amended) A compound according to claim 1 wherein $R_2$ is phenyl, thien-2-yl, naphthyl, indol-2-yl, indol-6-yl, benzo[b]furan-5-yl, benzo[b]thiophen-2-yl or benzimidazol-2-yl (each of which is optionally substituted as defined in claim 1).

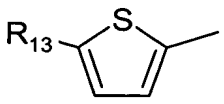
12. (amended) A compound according to claim 11 wherein optional substituents for $R_2$ are selected from: fluoro, chloro, bromo, iodo, nitro, thiol, difluoromethoxy, trifluoromethoxy, hydrazido, methylhydrazido, amino, cyano, trifluoromethyl, methylthio, vinyl, ethynyl, acetylamino, carboxy, acetoxy, hydroxy, methyl, ethyl, amido ($CONH_2$), aminomethyl, methoxy and ethoxy.

13. (amended) A compound according to claim 1 wherein $R_2$ is selected from one of the formula (A') to (H'):

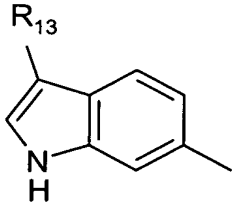
contd. A3



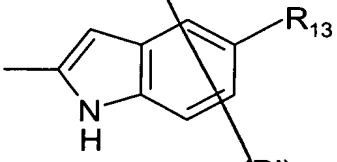

(A')



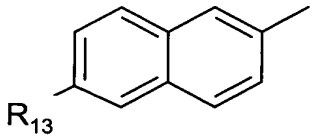

(B')



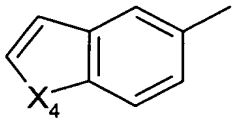

(C')



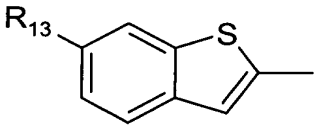

(D')



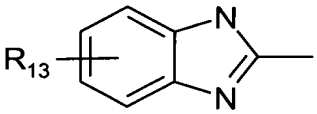

(E')




(F')




(G')




(H')

wherein $X_4$ is O or S, $R_{13}$ is selected from hydrogen, fluoro, chloro or methyl and $R_{14}$ is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and $R_{15}$ is selected from hydrogen, methyl, fluoro, chloro and amino.

14. (amended) A compound according to claim 1, wherein $R_2$ is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

15. (amended) A compound according to claim 1 wherein -X-X- is -CONH-.

contd. Q3 16. (amended) A compound according to any one of claims 1 to 15, 17 to 18 and 21 to 24 wherein Y is CH.

17. (amended) A compound according to claim 1 wherein Cy is an optionally $R_{3a}$ substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxazolyl, imidazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by $R_{3i}X_i$ in which $X_i$ is a bond, O, NH or $CH_2$ and $R_{3i}$ is phenyl, pyridyl or pyrimidinyl optionally substituted by $R_{3a}$.

Sub B1

18. (amended) A compound according to claim 1 wherein Cy is an optionally $R_{3a}$ substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group.

19. (cancelled on national phase entry)

20. (cancelled on national phase entry)

Q4 21. (amended) A compound according to claim 1 wherein $R_{3a}$ is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, $CONH_2$, $CH_2CONH_2$, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl, pyrrolidin-1-ylcarbonyl,

Sub B1

contd. cl 4

piperidin-1-ylcarbonyl, morpholin-1-ylcarbonyl and $-OCH_2O-$ (which is bonded to two adjacent ring atoms in Cy).

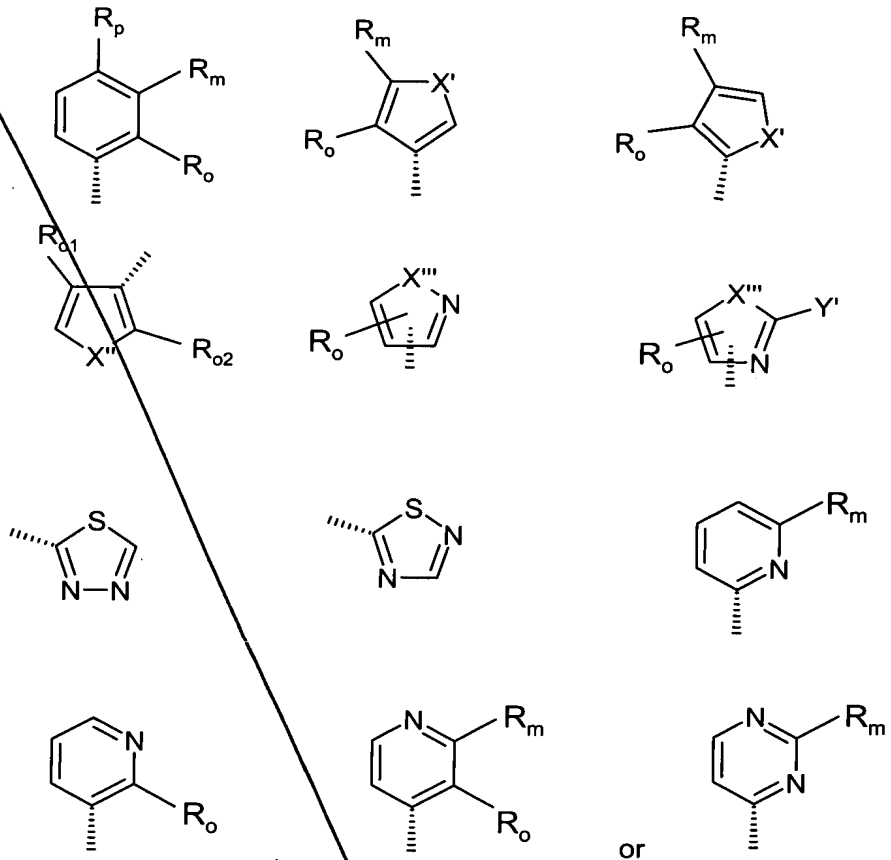
cl 5 cl 1

22. (amended) A compound according to claim 1 wherein $R_{3a}$ is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, $CONH_2$, $CH_2CONH_2$, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

23. (amended) A compound according to claim 1 wherein Cy is selected from:

contd. claim 4

Sub B1



or

wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

$R_o$ is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

$R_m$ is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein $X^3$ is O or S and $R^{11}$ and $R^{12}$ are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);

$R_p$ is selected from hydrogen and fluoro; or

contd. Q4

$R_o$ and $R_m$ or $R_m$ and $R_p$ form an $-OCH_2O-$ group; or $R_o$ and $R_m$ together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroary ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur);

one of $R_{o1}$ and $R_{o2}$ is hydrogen and the other is $R_o$.

Sub B1

24. (amended) A compound according to claim 1 wherein Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-3-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, naphthyl, isoquinolin-5-yl, isoquinolin-8-yl, quinolin-4-yl, quinolin-5-yl, and quinolin-8-yl.

25. (amended) A compound as claimed in Claim 16, in which the alpha atom in Y is carbon and has the conformation that would result from construction from a D-α-aminoacid $NH_2-CR_{1b}(Cy)-COOH$ where the $NH_2$ represents part of X-X

26. (amended) A pharmaceutical composition, which comprises a compound as claimed in claim 1 together with at least one pharmaceutically acceptable carrier or excipient.

27. (cancelled on national phase entry).

28. (cancelled on national phase entry).

Q5 Sub B1

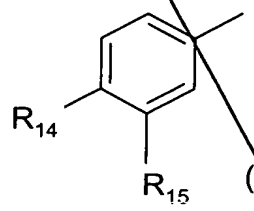
29. (amended) A method of treatment of a human or non-human animal body to combat a thrombotic disorder, which comprises administering to said body an effective amount of a compound as claimed in claim 1, but including the compound 4-[(3-ethoxybenzoyl-D,L-phenylglycinyl)aminomethyl]-1-[4-chlorobenzyl]piperidine.

30. (cancelled on national phase entry).

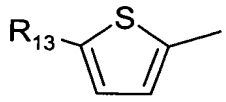
31. (cancelled on national phase entry).

32. (New) A compound according to Claim 1 wherein:

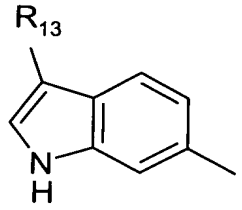
$R_2$ is is selected from one of the formula (A') to (H'):



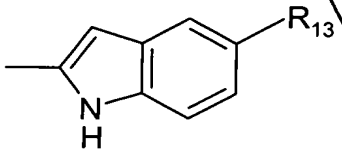

(A')



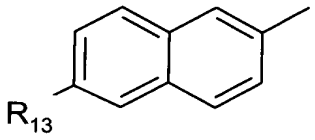

(B')



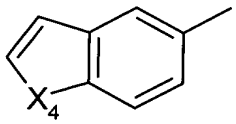

(C')



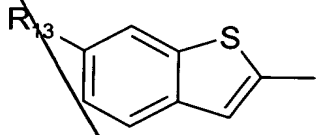

(D')



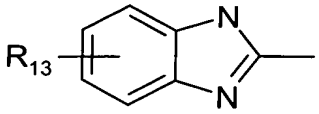

(E')




(F')




(G')




(H')

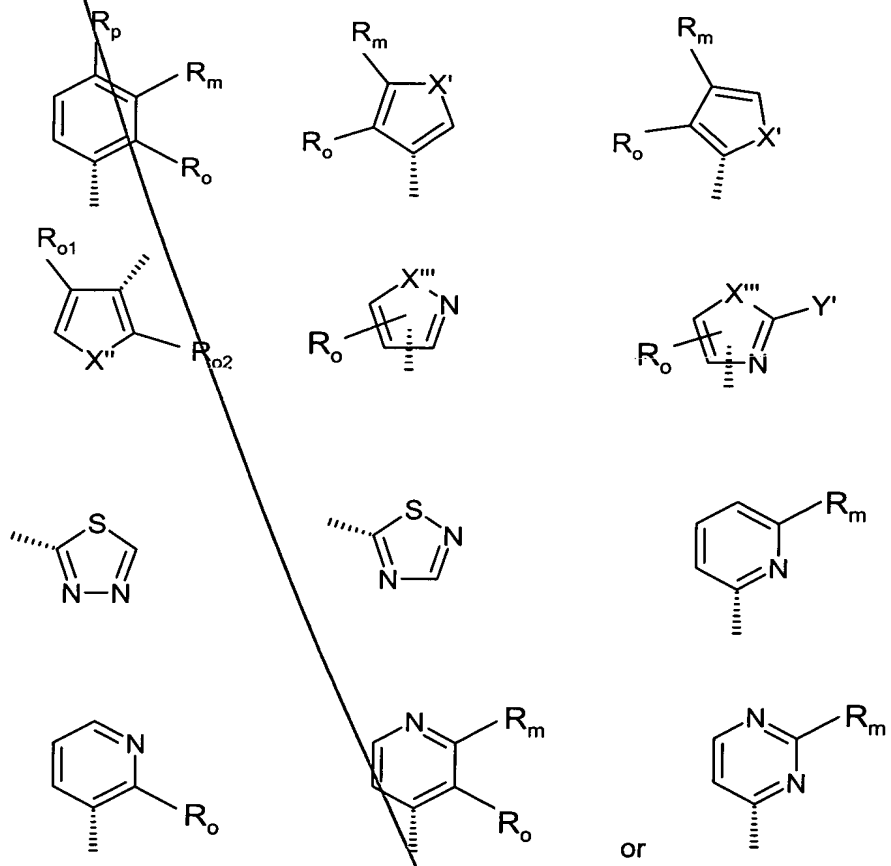
wherein $X_4$ is O or S, $R_{13}$ is selected from hydrogen, fluoro, chloro or methyl and $R_{14}$ is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and $R_{15}$ is selected from hydrogen, methyl, fluoro, chloro and amino;

X-X represents CONH;

contd.

Y (the α-atom) is CH and has the conformation that would result from construction from a D-α-aminoacid $NH_2$-$CR_{1b}$(Cy)-COOH where the $NH_2$ represents part of X-X;

Cy is selected from:



or

wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

$R_O$ is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

$R_m$ is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl,

contd. claim 6

methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein $X^3$ is O or S and $R^{11}$ and $R^{12}$ are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);

$R_p$ is selected from hydrogen and fluoro; or

$R_o$ and $R_m$ or $R_m$ and $R_p$ form an $-OCH_2O-$ group; or

$R_o$ and $R_m$ together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroary ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur);

one of $R_{o1}$ and $R_{o2}$ is hydrogen and the other is $R_o$; and

L is CONH, $CH_2NHCO$, $CONHCH_2$, $CONHCH_2CH_2$ or $CON(Me)CH_2$.

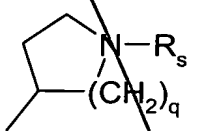
Sub B1

33. (New) A compound according to Claim 32 wherein

$R_2$ is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl;

Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-3-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, naphthyl, isoquinolin-5-yl, isoquinolin-8-yl, quinolin-4-yl, quinolin-5-yl, and quinolin-8-yl; and

$Lp(D)_n$ is of the formula:




wherein:

q is 1 or 2;

$R_s$ is hydrogen, $-(CH_2)_c-R_c$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [c is 0, 1 or 2; wherein $R_c$ is pyridyl or phenyl (which phenyl may

contd. Cl 6

bear a fluoro, chloro, methyl, $CONH_2$, $SO_2NH_2$, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and $R_e$ and $R_f$ are independently hydrogen or $C_{1-3}$alkyl; or $CHR_eR_f$ is (3-6C)cycloalkyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position, provided the substituent is not bonded to the CH group which is bonded to L), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl (which may bear a 1-methyl substituent), piperidinyl (which may bear a 1-methyl substituent) (provided that the tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and piperidinyl rings are not linked to the piperidin-1,4-diyl group through a ring nitrogen atom or a ring carbon atom adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-2-yl].

Such Cl

34. (New) A compound according to Claim 2 wherein $R_2$ represents:

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy, $MeSO_2$-, hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl, methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl;

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;

contd. A6

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

Sub B1

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl substituted at the 5 position by methyl;

(ix) pyrid-2-yl optionally substituted at the 6 position by chloro;

(x) pyrid-3-yl optionally substituted at the 4 position by chloro;

(xi) benzofur-2-yl optionally substituted at the 3 position by chloro, methyl or methoxy, at the 5 or 6 position by methyl and at the 6 position by methoxy;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;

(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy;

X-X represents CONH;

Y (the α-atom) is CH and has the conformation that would result from construction from a D-α-aminoacid $NH_2$-$CR_{1b}$(Cy)-COOH where the $NH_2$ represents part of X-X;

Cy is an optionally $R_{3a}$ substituted phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group;

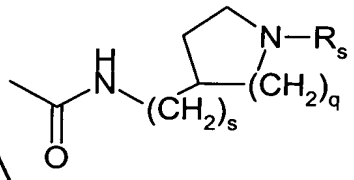
$R_{3a}$ is selected from hydrogen, hydroxyl, methoxy, ethoxy,

contd. cl 6

methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, $CONH_2$, $CH_2CONH_2$, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl; and

Sub cl

$-L-Lp(D)_n$ is of the formula:



wherein

q is 1 or 2;

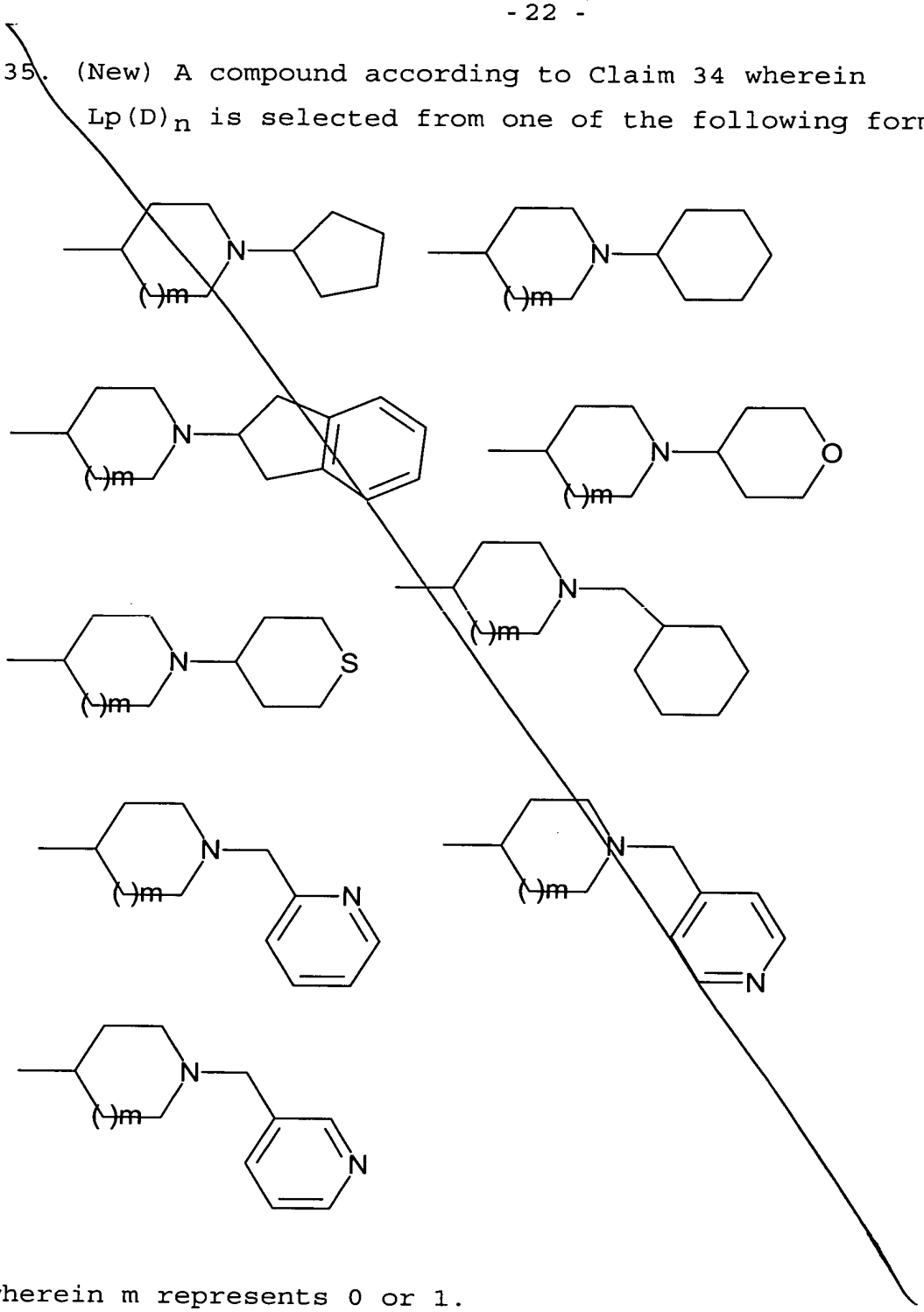
s is 0 or 1; and

$R_S$ is $-(CH_2)_c-R_C$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [wherein c is 1 or 2; $R_C$ is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, $SO_2NH_2$, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and $R_e$ and $R_f$ are independently hydrogen or $C_{1-3}$alkyl; or $CHR_eR_f$ is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substitutent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

contd. 6

35. (New) A compound according to Claim 34 wherein $Lp(D)_n$ is selected from one of the following formulae:

Sub B1



wherein m represents 0 or 1.